



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 862

[Docket No. FDA-2016-P-1026]

Medical Devices; Exemption From Premarket Notification: Method, Metallic Reduction, Glucose (Urinary, Nonquantitative) Test System in a Reagent Tablet Format

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is publishing an order denying a petition requesting exemption from the premarket notification requirements for “method, metallic reduction, glucose (urinary, nonquantitative)” devices that are in a reagent tablet format and are classified as class II devices as urinary glucose (nonquantitative) test system (hereinafter referred to as “copper reduction tablet test”). Urinary glucose (nonquantitative) measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, hypoglycemia, and hyperglycemia. FDA is publishing this order in accordance with procedures established by the Food and Drug Administration Modernization Act of 1997 (FDAMA).

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Sheila Connors, Center for Devices and Radiological Health (CDRH), Food and Drug Administration, 10903 New Hampshire Ave.,

Bldg. 66, rm. 4620, Silver Spring, MD 20993-0002, 301-796-6181,
Sheila.Connors@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Statutory Background

Under section 513 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360c), FDA must classify devices into one of three regulatory classes: Class I, class II, or class III. FDA classification of a device is determined by the amount of regulation necessary to provide a reasonable assurance of the safety and effectiveness of the device. Under the Medical Device Amendments of 1976 (1976 amendments) (Pub. L. 94-295), as amended by the Safe Medical Devices Act of 1990 (Pub. L. 101-629), devices are to be classified into class I (general controls) if there is information showing that the general controls of the FD&C Act are sufficient to assure safety and effectiveness; into class II (special controls) if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide such assurance; and into class III (premarket approval) if there is insufficient information to support classifying a device into class I or class II and the device is a life sustaining or life supporting device, or is for a use which is of substantial importance in preventing impairment of human health or presents a potential unreasonable risk of illness or injury.

Section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and the implementing regulations (21 CFR part 807) require persons who intend to market a device intended for human use to submit a premarket notification (510(k)) to FDA containing information that allows FDA to determine whether the device is “substantially equivalent” within the meaning of section 513(i) of the FD&C Act to a legally marketed device that does not require premarket approval (PMA).

On November 21, 1997, the President signed into law FDAMA (Pub. L. 105-115). Section 206 of FDAMA, in part, added a new section, 510(m), to the FD&C. Section 510(m)(1) of the FD&C Act requires FDA, within 60 days after enactment of FDAMA, to publish in the Federal Register a list of each type of class II device that does not require a report under section 510(k) to provide reasonable assurance of safety and effectiveness. Section 510(m) of the FD&C Act further provides that a 510(k) will no longer be required for these devices upon the date of publication of the list in the Federal Register. FDA published that list in the Federal Register of January 21, 1998 (63 FR 3142).

Section 510(m)(2) of the FD&C Act provides that 1 day after the date of publication of the list under section 510(m)(1), FDA may exempt a class II device on its own initiative or upon petition of an interested person if FDA determines that a 510(k) is not necessary to provide a reasonable assurance of the safety and effectiveness of the device. This section requires FDA to publish in the Federal Register a notice of intent to exempt a device, or of the petition, and to provide a 30-day comment period. Within 120 days of publication of this document, FDA must publish in the Federal Register its final determination regarding the exemption of the device that was the subject of the notice. If FDA fails to respond to a petition under this section within 180 days of receiving it, the petition shall be deemed granted.

FDA classified the urinary glucose (nonquantitative) test system into class II effective July 30, 1987 (52 FR 16102 at 16122, May 1, 1987). The classification for urinary glucose (nonquantitative) test system is at § 862.1340 (21 CFR 862.1340). The urinary glucose (nonquantitative) test system is identified as a device that is intended to measure glucosuria (glucose in urine). Urinary glucose (nonquantitative) measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, hypoglycemia,

and hyperglycemia. Devices under this classification regulation require premarket notification under section 510(k) of the FD&C Act.

II. Criteria for Exemption

There are a number of factors FDA may consider to determine whether a 510(k) is necessary to provide reasonable assurance of the safety and effectiveness of a class II device. These factors are discussed in the guidance the Agency issued on February 19, 1998, entitled “Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff” (Ref. 1). Accordingly, FDA generally considers the following factors to determine whether premarket notification is necessary: (1) The device does not have a significant history of false or misleading claims or risks associated with inherent characteristics of the device; (2) characteristics of the device necessary for its safe and effective performance are well established; (3) changes in the device that could affect safety and effectiveness will either (a) be readily detectable by users by visual examination or other means such as routine testing, before causing harm, or (b) not materially increase the risk of injury, incorrect diagnosis, or ineffective treatment; and (4) any changes to the device would not be likely to result in a change in the device’s classification. FDA may also consider that, even when exempting devices, these devices would still be subject to the limitations on exemptions.

III. Petition

On March 18, 2016, FDA received a petition requesting an exemption from premarket notification requirements for copper reduction tablet tests that are classified as class II devices under § 862.1340, urinary glucose (nonquantitative) test system, from Martin O’Connor, Germaine Laboratories, Inc. (See Docket No. FDA-2016-P-1026).

On May 4, 2016 (81 FR 26802), FDA published a notice in the Federal Register announcing that this petition had been received in accordance with section 510(m)(2) of the FD&C Act. On June 20, 2016 (81 FR 39929), FDA republished a notice of the petition due to an inadvertent error in the docket number and provided an opportunity for interested persons to submit comments on the petition by July 20, 2016. FDA received no comments regarding this petition.

FDA has completed review of the referenced petition and assessed the need for 510(k) clearance for copper reduction tablet test against the criteria laid out in section II. For the reasons described in this document, FDA has determined that premarket notification is necessary to provide a reasonable assurance of the safety and effectiveness of the copper reduction tablet tests classified under § 862.1340 and assigned the classification product code JIM. Accordingly, FDA responded to the petition by letter dated September 6, 2016, denying the petition within the 180-day timeframe under section 510(m)(2) of the FD&C Act. (See Docket No. FDA-2016-P-1026).

IV. Order

After reviewing the petition, FDA has determined that the petition failed to provide information to demonstrate that premarket notification is not necessary to provide a reasonable assurance of the safety and effectiveness of the device. Accordingly, FDA is denying the referenced petition for exemption from the premarket notification requirements.

With regard to the first factor (see section II, Criteria for Exemption), although there have been no medical device reports reported to the Agency in recent years, there have been numerous reports to the Agency¹ and in medical literature of risks associated with the inherent

¹ For more information, see Medical Device Reporting (MDR) database at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM>.

characteristics of this device, including possible device-associated deaths, serious injuries, and malfunctions such as burns, explosions of the product bottle due to heat, and consumption of the device. For instance, there have been reports in the medical literature of patients consuming the tablets because of their similarity to pills, which has led to poisoning and one report of a death. Therefore, FDA does not agree with the petitioner that the device does not have a significant history of risks associated with inherent characteristics of the device.

Additionally, failure to observe the reaction at all times after the tablet has been added to the sample is another risk associated with the inherent characteristics of the device. This can lead to a false-negative result and result in improper patient management, which can lead to serious injury or possibly death. The petition does not address how the device's inherent risks can be mitigated or controlled without premarket notification to provide a reasonable assurance of the safety and effectiveness of the device.

With regard to the second factor, the petition stated that healthcare and laboratory professionals understand the appropriate use of a copper reduction tablet test and that a definitive diagnostic or therapeutic decision should not be based on the result of this method. However, a copper reduction tablet test can be used to evaluate pediatric patients for possible hereditary metabolic disorders through detection of reducing substances. For example, although all States require mandatory newborn screening for genetic metabolic defects, clinical laboratories may still use this device as a screening test on pediatric urine samples if there are any suspicions of metabolic disease prior to receiving newborn screening results or if the newborn screening results do not match the clinical state of the newborn. Although further diagnostic testing may be performed to confirm the result(s), physicians may immediately treat the newborn relying solely on the result of this test while awaiting the results for any followup diagnostic tests. False

negative results also present a safety and effectiveness concern because followup diagnostic testing may not be performed, leading to the failure to start needed treatment for the newborn. The petition failed to demonstrate that a premarket submission is not necessary to provide a reasonable assurance of the safety and effectiveness of the device for such uses, and FDA does not agree that the characteristics of the device necessary for its safe and effective use are well established.

With regard to the third factor, FDA also does not agree that changes in the device that could affect safety and effectiveness will either be readily detectable or not materially increase risks. The petition claimed that users could employ positive or negative controls to validate the reagents performance. However, while available quality control materials may contain glucose, they do not contain other reducing sugars (e.g., galactose, lactose). Therefore, such materials might not readily detect an issue with the device's safety or effectiveness in detecting other reducing sugars before causing harm. The petition argued that well-established protocols and methods could ensure there is no material increase in risk. The petition provided insufficient information to support this argument that changes in the device that could affect safety and effectiveness will either be readily detectable or not materially increase risks. Moreover, changes in the device that could affect safety and effectiveness might materially increase the risk of injury, incorrect diagnosis or ineffective treatment given the device type's intended uses. The petition also did not provide information to the contrary. The petition did not provide any relevant information regarding the fourth factor.

In addition to these four factors, FDA considers the "limitations on exemption." Manufacturers of any commercially distributed device for which FDA has granted an exemption from the requirement of premarket notification must still submit a premarket notification to FDA

prior to marketing the device when any of the limitations of exemption are exceeded. The general limitations of exemption from premarket notification contained in § 862.9 (21 CFR 862.9) are broadly applicable to in vitro diagnostic (IVD) devices classified under part 862 (21 CFR part 862). Under § 862.9, the exemption from the premarket notification requirements applies, in the case of IVD devices, only to those devices under part 862 for which misdiagnosis, as a result of using the device, would not be associated with high morbidity or mortality. FDA has previously assessed that this limitation is exceeded, and a premarket notification is necessary to provide a reasonable assurance of the safety and effectiveness of an IVD device, when such device is intended for use in screening or diagnosis of familial or acquired genetic disorders, including inborn errors of metabolism (§ 862.9(c)(2)) or intended for use in diabetes management (§ 862.9(c)(5)). The petition argued that the copper reduction tablet test is not intended for use in screening or diagnosis of familial and acquired genetic disorders, including inborn errors of metabolism, or for use in diabetes management. However, as explained previously, FDA disagrees and believes that the copper reduction tablet test described in the petition is intended for such uses and would likely exceed the limitations previously mentioned.

Accordingly, for all of the foregoing reasons, the petition failed to demonstrate that a premarket submission is not necessary to provide a reasonable assurance of the safety and effectiveness of the device intended for such uses. Therefore, FDA is issuing this order denying the petition requesting exemption for a method, metallic reduction, glucose (urinary, nonquantitative) test system in a reagent tablet format that is intended to measure glucosuria (glucose in urine) from the premarket notification requirements. Manufacturers of this device type must continue to submit and receive FDA clearance of a 510(k) before marketing their device, as well as comply with all other applicable requirements under the FD&C Act.

V. Reference

The following reference is on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and is available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; it is also available electronically at <http://www.regulations.gov>. FDA has verified the Web site address, as of the date this document publishes in the Federal Register, but Web sites are subject to change over time.

1. “Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff,” February 1998, available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080199.pdf>.

Dated: September 28, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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